

Postpartum depression: we know the risks, can it be prevented?

Depressão pós-parto: sabemos os riscos, mas podemos preveni-la?

Dawn Zinga,¹ Shauna Dae Phillips,^{2,3}
Leslie Born^{3,4}

Abstract

In the past 20 years, there has been increasing recognition that for some women, pregnancy may be burdened with mood problems, in particular depression, that may impact both mother and child. With identification of risk factors for postpartum depression and a growing knowledge about a biologic vulnerability for mood change following delivery, research has accumulated on attempts to prevent postpartum depression using various psychosocial, psychopharmacologic, and hormonal strategies. The majority of psychosocial and hormonal strategies have shown little effect on postpartum depression. Notwithstanding, results from preliminary trials of interpersonal therapy, cognitive-behavioural therapy, and antidepressants indicate that these strategies may be of benefit. Information on prevention of postpartum depression using dietary supplements is sparse and the available evidence is inconclusive. Although a few studies show promising results, more rigorous trials are required. The abounding negative evidence in the literature indicates that postpartum depression cannot be easily prevented, yet.

Keywords: Depression, postpartum/drug therapy; Puerperal disorders/psychology; Depression/psychology; Antidepressive agents/therapeutic use; Adaptation, psychological; Mother-child relations; Women's health

Resumo

Nos últimos vinte anos, houve um maior reconhecimento de que a gravidez em algumas mulheres pode ser complicada por problemas emocionais, particularmente depressão, causando um impacto significativo sobre a mãe e a criança. Com a identificação de fatores de risco para a depressão pós-parto e um aumento do conhecimento sobre a vulnerabilidade biológica para os transtornos de humor no período puerperal, um número crescente de estudos tem explorado meios de prevenir a depressão pós-parto, utilizando estratégias psicossociais, psicofarmacológicas e hormonais. A maior parte das intervenções psicossociais e hormonais tem mostrado pouco efeito para a prevenção da depressão pós-parto. Apesar disso, resultados de estudos preliminares sobre a terapia interpessoal, terapia cognitivo-comportamental e sobre o uso de antidepressivos indicam que estas intervenções podem resultar em algum benefício. Dados sobre o uso de suplementos dietéticos são limitados e com resultados pouco conclusivos. A excessiva quantidade de resultados negativos na literatura atual demonstra que a depressão pós-parto ainda não pode ser facilmente prevenida.

Descritores: Depressão pós-parto/quimioterapia; Transtornos puerperais/psicologia; Depressão/psicologia; Antidepressivos/uso terapêutico; Adaptação psicológica; Relações mãe-filho; Saúde da mulher

¹ Department of Child and Youth Studies, Brock University, St. Catharines, Ontario, Canada

² Women's Health Concerns Clinic, St. Joseph's Healthcare, Hamilton, Ontario, Canada

³ Medical Sciences Program, McMaster University, Hamilton, Ontario, Canada

⁴ Motherisk Program, The Hospital for Sick Children, Toronto, Ontario, Canada

Correspondence

Dawn Zinga
Department of Child and Youth
Brock University
St. Catharines, Ontario, Canada L2S 3A1
Phone: (905) 688-5550, ext. 3152 Fax: (905) 641-2509
E-mail: dzinga@brocku.ca

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Introduction

In the past 20 years, there has been increasing recognition that for some women, pregnancy may be burdened with mood problems, in particular depression. This insight runs contrary to the wide-held popular belief that pregnancy is a joyous time for all women. Investigators have also recognized that problems with mood during pregnancy place women at risk for postpartum depression (PPD). Consequently, there has been a shift in the literature from a focus strictly on symptoms and treatment of PPD to the treatment of depression or anxiety during pregnancy, in order to obviate a worsening of symptoms during the postpartum period. In the past several years, there has been a host of studies that have aimed at preventing the occurrence of PPD, which included women who were identified as at risk for PPD and euthymic during pregnancy or symptomatic.

This paper will review the current literature on the etiology of and risk factors for PPD, and the psychosocial and pharmacologic strategies that have been tried in effort to prevent its onset in women at risk.

Prevalence of depression in pregnancy

It is estimated that 25%-35% of women experience depressive symptoms during pregnancy, and up to 20% of women may meet criteria for depression.¹⁻³ Rates of depressive symptoms have been found to be higher during the third trimester than at six-months postpartum.⁴ During pregnancy, however, investigators have found a peak in depression in the first trimester, an amelioration of symptoms during the second trimester, and an increased rate of depression during the third trimester.^{2-3,5}

Increasing literature shows that psychiatric disorders during pregnancy are under-detected and under-treated in clinical practice. Marcus et al prospectively screened 3,472 pregnant women in several obstetrical settings for depression (Center for Epidemiological Studies-Depression scale [CES-D]), use of antidepressant medications, past history of depression and current treatment, including medication, psychotherapy, or counseling.⁶ Of the women screened, 20% (n = 689) met the cutoff score for depression on the CES-D. Only 13.8% (n = 95) of the women meeting the cutoff CES-D score reported receiving any type of formal treatment for depression.

1. Prevalence of postpartum mood disorders

Eight out of ten women may experience the postpartum blues, a transient disturbance of mood typically marked by mood lability, occasions of crying, irritability, and sleep disturbance that lasts about two weeks postpartum.⁷ In some women, the depressive symptoms do not resolve but persist and lead to post-partum depression.⁸

Epidemiologic studies have identified the prevalence of postpartum depression (PPD) as ranging between 10% and 20%.⁹ Approximately one in every 1,000 deliveries is followed by a psychotic episode.¹⁰

2. Relevance of mood to maternal and infant wellbeing

Depression during pregnancy is associated with diminished prenatal care, including poor nutrition and irregular sleeping habits. A small Michigan study, with a diverse ethnic sample, revealed that approximately 15% of women (n = 169) reported alcohol use during pregnancy.¹¹ Recent additional evidence shows that alcohol consumption is positively and linearly correlated with antenatal depression.¹² Binge drinking during pregnancy is also associated with smoking.¹¹

In a sample of 1,399 low-income African-American women, 117 women had a preterm birth. Among these women, spontaneous preterm birth occurred in 12.7% of those with maternal depressive symptoms and 8% without depressive symptoms according to the CES-D.¹³ Results from Dole et al indicate that high maternal anxiety is also associated with preterm birth.¹⁴ Of 1962 women, preterm birth occurred in 231 cases. 42% of women with high prenatal anxiety had preterm deliveries, compared with 29% with high prenatal anxiety that gave birth at term. Although depression in this study was not a significant factor in preterm births, it may increase the propensity of preterm births in African-American women, a population more vulnerable to spontaneous preterm births.¹⁵

PPD has been linked with disruptions in mother-infant dyadic functioning, such as mutual attentiveness, vocal and visual communication, less frequency of interactions involving touch and smiling as compared with dyads including non-depressed mothers.¹⁶⁻¹⁷ Depressed mothers have also demonstrated more intrusive and irritated behavior towards their infants, and respond less sensitively, less contingently, and more negatively to their infants.^{16,18}

Infants and young toddlers may be particularly vulnerable to the negative effects of PPD.¹⁹ Research has shown that children of women with PPD display higher rates of insecure attachment, some delays in cognitive and emotional development, and more dysphoria.²⁰

Despite findings that the decreased maternal functioning associated with PPD disappear by the 16th postpartum month,¹⁶ there is growing evidence to suggest that there may be long term implications for children's development.²¹ In addition, the severity and chronicity of maternal depression clearly predicts developmental difficulties.^{19-20,22}

Etiology of postpartum depression

Current thinking suggests that some women have a particular sensitivity to hormonal changes, beginning at the onset of menarche, which increases their vulnerability to psychological, environmental, and physiological stressors during the reproductive years.⁷ In susceptible women, these stressors trigger a change from an already vulnerable state to the manifestation of a female-specific mood disorder at times of high hormonal fluctuations such as parturition.

1. The hormonal withdrawal theory

The most intriguing evidence for a significant hormonal role has been demonstrated by an experiment that simulated supraphysiological levels of estradiol and progesterone in late pregnancy and subsequent withdrawal (i.e., parturition), in women with or without a history of PPD.²³ Depression scale scores were significantly higher during the hormonal withdrawal phase in women with a prior history of PPD, while the group with no history showed minimal change in mood scores. There was a subsequent improvement in mood rating in the former group with returning ovarian function.

Reciprocal interactions between the hypothalamic-pituitary-gonadal (HPG) axis and central serotonergic system have been demonstrated. The low gonadal steroid levels typical of the puerperium may decrease central serotonergic activity and confer an increased vulnerability to the development of mood symptoms in susceptible women. One line of thinking is that postpartum mood disturbance may be subverted by "adjusting" the hormonal levels or by "reversing" the sensitivity of the neurotransmitter system.²⁴ One prophylactic pilot trial,

discussed below, attempted somewhat successfully to 'cushion' the dramatic drop in estradiol after parturition.

2. Genetic studies

A biological component of postpartum mood disorders is suggested by family history and twin studies. The lifetime prevalence of mood-related disorders in the first-degree relatives of women with postpartum mood disorders is much higher than in the general population, which indicates a potential genetic or familial component of the disorders.²⁵

Evidence from studies of premenstrual dysphoria has shown that the serotonergic system is in close reciprocal relationship with gonadal hormones.⁷ There is preliminary evidence of a genetic predisposition to altered activity of the serotonin transporter system in women with severe premenstrual dysphoria (M Steiner, unpublished data). A serotonin transporter-linked promoter polymorphism (5-HTTLPR) has been linked with major depression.²⁶ While the reciprocal relationship between the serotonergic system and gonadal hormones has not as yet been studied in pregnant or postpartum women, it is plausible that the sudden estrogenic withdrawal at parturition may be a trigger for mood change in genetically vulnerable women.

Risk factors for postpartum depression

The literature consistently shows that a personal or family history of psychiatric illness can increase the risk for severe postpartum emotional disturbance. This includes a personal psychiatric history of mood or anxiety disorders including premenstrual syndrome or sexual abuse;^{25,27-28} a family history of psychiatric disorder including alcoholism, PPD, or postpartum psychosis.^{25,29} In a prospective controlled study, Cooper and Murray found that 41% of their subjects experienced a subsequent episode of PPD after a first (index) episode of depression with postpartum onset.³⁰

Depressed or anxious mood during pregnancy or symptoms of elation in the early puerperium are associated with subsequent PPD,^{1,29} as are neurotic or vulnerable personality traits.²⁹ Depressed women who binge-drink or smoke during their pregnancies are at a higher risk of their depression continuing into the postpartum period.³¹ The level of antenatal anxiety appears to be positively correlated to the level of postnatal depression.³²

Although antepartum and postpartum depression can occur independently of each other and that distinct psychoneuroendocrine profiles exist,³³ it has been suggested that many of the postpartum mood disorders may actually begin during pregnancy or that antepartum depression increases the risk of developing PPD.³⁴

For some women, especially primiparous mothers, the transition to motherhood may be difficult and compounded by low self-esteem,³⁵ particularly if the pregnancy was unplanned.³⁶ Women who are socially isolated from family, friends or their partner are more likely to experience postpartum depressive symptoms.³⁷ This may be especially true for women who are recent immigrants experiencing geographic and language barriers.³⁸ Other negative life events such as the loss of a job or the death of a close family member are also predictive of PPD.²⁹

Associations have also been found with the presence of obstetric complications, such as antepartum hemorrhage or emergency caesarean section; or sleep deprivation across late pregnancy, parturition and the immediate postpartum period

and an increased risk for PPD.^{29,39-40} Infant factors such as child temperament, childcare stress, or neonatal complications have also been associated with the onset of postpartum depressive symptomatology.³⁵

Controversy exists as to how well the identification of risk factors enables clinicians or investigators to distinguish between those women who will go on to become depressed and those who will remain well. PPD prevention trials and related evidence from untreated control groups have shown that screening tools do identify women at high risk for PPD, however the effectiveness of the screens is questionable as they often misidentify women as well.⁴¹

With the identification of risk factors for PPD, the past decade has witnessed an increased amount of research on preventive strategies. In the following sections, psychosocial, psychopharmacologic, and hormonal preventive strategies will be reviewed.

Psychosocial strategies

A number of trials using psychosocial strategies have attempted to prevent the development of PPD by alleviating or eliminating the psychosocial risk factors. These interventions have mainly taken the form of educational initiatives, enhancements to healthcare during pregnancy and/or early puerperium, and psychotherapeutic approaches.

1. Educational initiatives

Educational initiatives operate on the premise that providing individuals or families with information about what to expect in the postpartum period will reduce anxiety levels and thus help reduce the impact of psychosocial risk factors. Some research has associated antenatal education with reductions in anxiety and the perception of benefit by participating women,⁴² while other research has found no reduction in anxiety.⁴³ In general, antenatal educational interventions have not been shown to be very effective in reducing PPD.

In an early randomized, controlled trial, Australian women were assigned to receive either routine antenatal care or the addition of two antenatal classes and one postnatal class. There were no differences between the two groups on depressive symptoms as measured by the Edinburgh Postnatal Depression Scale (EPDS) at 6 weeks, 3 months, and 6 months postpartum.⁴⁴ Another Australian study failed to find any significant differences in PPD scores between women randomized to standard antenatal classes or "intervention" antenatal classes that focused on emotional issues and the reality of parenthood as well as physical preparation, although a decrease in anxiety was observed for the intervention group.⁴⁵

A third Australian study used a three-tiered approach by first identifying women at risk, then providing education, and finally notifying the physicians about each woman's at risk status.⁴⁶ Women who were identified as at-risk were randomly assigned to either the treatment or to standard care. Those in the treatment group received an educational booklet on PPD and resource telephone numbers; in addition, their care providers received a letter alerting them to the woman's risk status. There were no significant differences in scores on the EPDS between the two groups at 16 weeks postpartum.

In the "Preparing for Parenthood" study, women identified as at-risk for PPD were randomly assigned to receive routine care or participate in the six antenatal group education classes (topics included social and emotional problems of pregnancy, post-natal depression, support skills, problem-solving).⁴⁷ There

were no significant differences between the two groups at 3 months postpartum. Notably, 55% of women in the intervention group did not complete the six classes.

Hayes et al implemented an educational approach in which women at 28-36 weeks gestation were randomly assigned to routine antenatal care, or provided with an educational package containing an information booklet for expectant women and their families and an audiotape of one woman's experience of PPD as told to a midwife.⁴⁸ The results showed that there were no significant differences between the groups at 8-12 and 16-24 weeks postpartum. Both groups were significantly more depressed antenatally than postnatally.

Two studies addressed the issue of antenatal prevention and its connection with the postpartum period. Tam et al focused on women who experienced pregnancy complications resulting in hospitalization, caesarean section, or birth complications.⁴⁹ Women were recruited within 48 hours following birth and then randomly assigned to either routine care or educational counselling, which included a full explanation of the suboptimal outcome, a discussion of the woman's emotional response, and an opportunity to come to term with the event and find solutions as necessary. At 6 weeks and 6 months postpartum, there were no significant differences in psychological morbidity, client satisfaction or quality of life between groups.

In a second controlled trial, women identified as being "vulnerable" were randomly assigned to either a treatment group (five antenatal monthly group meetings and six postnatal monthly meetings) or a control condition.⁵⁰ While second-time mothers showed no benefits from the treatment, primiparous mothers in the treatment group showed fewer depressive symptoms than those in the control group. The results of this latter study suggest that bridging the antenatal and postpartum periods may enhance the effectiveness of educational initiatives.

2. Enhanced ante/Postnatal care

Another approach in the struggle to prevent PPD has been targeted at maternal healthcare providers. The rationale underlying this approach is that increasing the level of healthcare during the antenatal period and/or the early postpartum, may in turn reduce the impact of psychosocial risk factors on postpartum mood. Yet, completed trials of enhanced maternal care have shown to have had limited impact on the prevention of PPD.

One randomized controlled trial provided families with a program of child-health nurse visits that occurred weekly from birth until 6 weeks postpartum, then bi-weekly until the third postpartum month and monthly until 6 months postpartum,⁵¹ with the aim of reducing poor health and developmental outcomes for *children* of women who reported environmental risk factors (i.e. domestic violence, low family income, history of mental disorder). The control group received standard postpartum care that included one optional home visit and unlimited access to the child-health centre by appointment. The results showed significantly lower scores on the EPDS and higher levels of parent-infant attachment for the intervention group as compared with the control group.

Another randomized controlled trial examined whether the addition of a postnatal check-up with the general practitioner one week after discharge would improve maternal health.⁵² The results showed there were no differences between the intervention and control groups on measures of depressive

symptoms, satisfaction with practitioner, breastfeeding rates, or number of problems reported by women.

Several other studies have also focused on alterations to maternal care in the early postnatal period to enhance the outcomes of women and their children. Morrell et al examined the cost effectiveness of implementing community postnatal supports in a community in the United Kingdom.⁵³ The community midwife randomly assigned women over seventeen years of age, who had live births and lived within the catchments area, to home visits from a postnatal support worker, in addition to the standard postnatal care at home by a midwife or to a control group who only received the standard care. While many of the women reported satisfaction with the increased support, there were no significant differences on EPDS scores or general health measures between groups.

A similar study in the West Midlands area of the United Kingdom looked at re-designing community postnatal care and found some statistically significant differences in EPDS scores between the control group and treatment group.⁵⁴ The treatment group received postnatal care individually tailored to each participant with flexible home visits (the last home visit at about 28 days postpartum) with a discharge visit at 10-12 weeks postpartum. The control group received routine care involving seven home visits by a midwife up to 10-14 days postpartum and a discharge visit at 6-8 weeks postpartum.

One randomized controlled study directly addressed the prevention of PPD through a program of continuous midwifery care throughout pregnancy and the postpartum.⁵⁵ Pregnant women with histories of major depressive disorder were randomized to standard care (8-12 antenatal midwifery visits, attendance at labour and delivery, and visits as required up to 10-28 postpartum days) or to continuous midwifery care by the same midwife (as much as possible) through pregnancy and postpartum. The investigators failed to find any differences in psychiatric outcomes between the two groups, but did find that continuous midwifery care was more effective in engaging women in treatment.

Other studies have added a debriefing/non-directive counselling session in the early postnatal period to women's standard postpartum care.⁵⁶⁻⁵⁸ However, in a recent review Gamble et al concluded that there was insufficient evidence to assess the effectiveness of debriefing sessions on the prevention of PPD, and two of the studies may have had harmful effects.⁵⁹

3. Psychotherapeutic approaches

In contrast to the mostly negative findings through educational initiatives and enhanced maternal healthcare, two preliminary studies using specific psychotherapeutic approaches have shown some promising results in efforts to prevent the occurrence of PPD.

One US study found that interpersonal therapy was effective in preventing PPD in a sample of at-risk women.⁶⁰ Expectant women (n = 37) who were identified at 20-32 weeks gestation as reporting at least one risk factor for PPD (i.e. previous depression, current depressive symptoms, poor social support) were randomly assigned to receive four "interpersonal-therapy-oriented" group sessions or standard care. Women in the treatment group reported significantly lower scores on the Beck Depression Inventory and none developed PPD in the first three postpartum months. In contrast, three of the women in the control group developed PPD, and the control group as a whole showed a significantly smaller change in the Beck Depression

Inventory Scores between 20-32 weeks gestation and three months postpartum.

In a second study conducted at 3 obstetric clinics in France, pregnant women with an EPDS score over 9 were randomly assigned either to the control or the intervention group. Women in both groups stayed in the clinic for three to five days and the intervention group differed from the controls as they received one cognitive-behavioural session during their stay. The intervention group showed significantly higher recovery rates and a significant reduction in the occurrence of "probable" depression.⁶¹ While the sample size was small and the intervention did not prevent PPD in all members of the intervention group, it did demonstrate that early intervention using a specific psychotherapeutic strategy among at-risk women could result in a significant reduction in depressive symptomatology.

Psychopharmacologic strategies

1. Antidepressant

1) Nortriptyline

Nortriptyline, a metabolite of the tricyclic antidepressant amitriptyline, is used as an antidepressive agent, in the treatment of major depression, dysthymia, and atypical depressions.

An early, open-label study of 23 women with a history of PPD showed that starting antidepressants within 24 hours of delivery was associated with a marked reduction of depression recurrence (1/15 women) compared with a group receiving monitoring only (5/8 women).⁶²

However, a subsequent double-blind placebo controlled study showed that prophylactic treatment with nortriptyline did not reduce rates of PPD. Women who were euthymic during the index pregnancy and had a prior history of PPD treated either with nortriptyline or placebo for 20 weeks, beginning within 24 hours of delivery. 6/26 subjects who took nortriptyline preventively and 6/25 placebo subjects suffered recurrences between 1 and 16 weeks postpartum. The time to recurrence did not differ between treatment groups. Between weeks 20 and 28, following discontinuation, an additional 3 subjects on nortriptyline and 1 subject on placebo had a recurrence of depression.⁶³

2) Sertraline

Sertraline is a widely used serotonin reuptake inhibitor that has been shown to have both antidepressant and anti-anxiety effects, and the data are positive for its use in lactating women.⁶⁴

In a pilot, placebo-controlled study, women with a history of PPD and who were euthymic during the index pregnancy received sertraline for a period of 20 weeks. The sertraline was initiated within hours of delivery, titrated over 4 weeks to a maximum dose of 75 mg/d, and discontinued at week 20 after tapering from week 17. Of the women who started sertraline (n = 14), one subject had a recurrence of PPD at week 17. A second subject had a recurrence of depression at week 20, and a third subject became depressed at week 26. In contrast, 4/8 placebo subjects suffered recurrence of PPD within the first 17 weeks of the study.⁶⁵ Based on the results, the authors recommended a minimum period of 26 weeks of preventive antidepressant treatment. Notwithstanding, a longer period of study is required.

It is important to consider that, when using antidepressants as prophylaxis against PPD, the timing of antidepressant administration has yet to be pinpointed. In women who are sensitive to hormonal changes, beginning antidepressant

therapy after hormonal changes have occurred may be too late for a prophylactic effect.

2. Dietary supplement

1) Calcium

In an ancillary study to a randomized controlled trial of calcium (2,000 mg of elemental calcium taken as calcium carbonate tablets) for prevention of preeclampsia, investigators found that women who received calcium supplementation during gestation had a statistically significant lower prevalence of PPD symptoms at 12 weeks following birth.⁶⁶ In the primary study, women (N = 4,589) received either 1,000 mg of calcium or placebo tablets with their morning and evening meals and a daily prenatal supplement (50 mg calcium, 30 mg iron, 400 IU vitamin D₂), beginning before 22 weeks gestation until delivery.⁶⁷ At 6 weeks postpartum, the mean EPDS scores were similar between treatment groups. At 12 weeks, the mean EPDS scores were not significantly different between the calcium and placebo groups. Yet, a significantly larger proportion of women in the placebo group (15.3%) had EPDS scores > 14 compared with the calcium treated group (5.7%) (p = 0.014).

While the exact mechanisms through which dietary calcium can influence negative affect are unknown, one line of thinking suggests that calcium supplementation may serve to directly or indirectly stabilize calcium regulation at the intracellular level in individuals with low calcium diets, which in turn helps to alleviate depression.⁶⁶ This has yet to be explored though in the context of PPD.

2) Omega-3 fatty acids

Fish oil, high in omega-3 fatty acids, has been used as a psychotropic medication for the treatment of major depression, either alone or as adjunct to antidepressant therapy, with mixed results. To-date, investigators have used ethyl eicosapentaenoic acid (EPA) or docosahexanoic acid (DHA) either alone or in combination. Preliminary studies revealed that women with a lower level of plasma DHA in late pregnancy and the early postpartum period may be more likely to experience postpartum depressive symptoms.⁶⁸ Thus, increasing the dietary DHA intake in late pregnancy or following delivery may reduce PPD symptoms.

One double blind randomized controlled study of DHA 200 mg/d for 4 months, beginning within a week after delivery, showed no statistical difference in measures of depression between groups at the four month mark, regardless of breastfeeding status. The authors noted that the women as a group (N = 51 DHA; N = 50 placebo) had "minimal depression symptoms" at baseline (BDI baseline mean score \pm standard deviation: 6.5 \pm 4.2 and 7.1 \pm 4.7 respectively).⁶⁹ There has been a suggestion in the literature that the dose used might have been insufficient for an antidepressant effect.⁷⁰

Another recent open-label pilot study (n = 7) of 2,960 mg of EPA and DHA in a 4:1 ratio, from 34-36 weeks of pregnancy to 12 weeks postpartum, taken by women with a prior history of PPD, showed that 4/7 subjects had a relapse of PPD, between 3 and 61 days postpartum.⁷¹

3. Hormonal

1) Thyroid

Investigators have demonstrated that thyroid peroxidase antibody positive women at 32 weeks gestation have a two-to-three-fold risk for the development of depression in the postpartum period.⁷²

Harris et al hypothesized that prophylactic administration of thyroxine would stabilize thyroid function following delivery, and in turn, prevent postnatal depression.⁷³ In a randomized double-blind study, 446 euthyroid women positive for thyroid peroxidase antibodies received 100 µg of thyroxine or a placebo daily from 6 to 24 weeks postpartum. The results failed to show a substantive clinical benefit of the treatment; the prevalence of depression was similar in both postpartum groups.

2) Estrogen

On the basis that the sudden and precipitous decline of hormones at parturition is a biologic trigger for mood changes in vulnerable women, one study explored whether cushioning the drop in estradiol in the hours after delivery would be effective as prophylaxis against PPD. Four euthymic women who had a prior episode of major depression with early postpartum onset were administered oral Premarin within hours of delivery, starting at 5 mg bid for 3 days (approximating term estradiol levels), and slowly tapered to follicular phase estradiol levels, with discontinuation after day 28. All four women remained well during the acute puerperium and for the first postpartum year.⁷⁴

Two additional studies have shown that oestrogen is an effective treatment for women diagnosed with moderate-severe major depression with postpartum onset.⁷⁵⁻⁷⁶ Ahokas and colleagues found that depression symptoms in women who received sublingual 17beta-estradiol rapidly decreased as their serum estradiol concentrations increased and approximated follicular phase levels,⁷⁵ findings which link to the previously mentioned hormonal withdrawal theory thought to underlie the development of PPD.

3) Progesterone

Progesterone prophylaxis against the development of PPD predated use of prophylactic estradiol by at least a decade, and initially the results appeared promising. The administration of progesterone immediately after delivery was hypothesized to help with women's "adjustment" to the rapid decline in progesterone after parturition. 94 women with a history of

PPD received 100mg intra muscular progesterone immediately after delivery, for 7 days, followed by progesterone suppositories 400 mg bid for 2 months or until the start of menses. PPD recurred in 9 women (about 10%), three of whom did not receive the recommended intervention dose. Dalton contrasted these results against an earlier case series in which 151/221 (68%) untreated women had a recurrence of PPD.⁷⁷

Yet, a subsequent randomized placebo-controlled study found that a single dose of depot norethisterone enantate, a synthetic progestogen, administered within 48 hours of delivery was associated with an *increased* risk of developing PPD. Further, significantly more women in the intervention group complained of vaginal bleeding.⁷⁸

Sleep

Women experience dramatic changes to their sleep pattern and sleep quality beginning in late pregnancy and extending well into the postpartum period, including frequent awakenings, fewer hours of total sleep, and shorter rapid eye movement sleep latency.⁷⁹ A recent prospective observational study has shown that women with severely disrupted sleep, i.e., less than 6 hours total sleep time per night, in the last month of pregnancy had longer labours and were more likely to have cesarean delivery.⁸⁰

Accumulating evidence underscores an association between sleep loss and negative mood in postpartum women.⁸¹ Women with nighttime labour have been demonstrated to be more susceptible to both negative mood in the first days postpartum, known as "baby blues",⁸² and to postpartum psychosis.⁸³ A significant relationship has been established between self-ratings of fatigue and self-ratings of depressive symptoms in the days after parturition.⁸⁴ Severe sleep deprivation is almost universally reported in women presenting for treatment of PPD.⁸⁵

Results of electroencephalographic sleep studies suggest that women at risk for developing PPD may show underlying differences in their sleep physiology, even when in remission.⁸⁶

Table 1 – Summary of prophylaxes showing promise against postpartum depression in women at risk

Category	Prophylaxis	Dose	Start	Duration	Comments	Reference
Enhanced Postnatal Care	Structured program of child health nurse visits	Home visits for six months postpartum	First postpartum week	Weekly – 0-6 wks Bi-weekly – 7-12 wks Monthly – 3-6 months	<ul style="list-style-type: none"> Randomized, controlled trial n = 91 Enhances maternal-infant attachment Prevents maternal mood disorder 	(51)
Psychotherapeutic	Interpersonal therapy oriented groups	60 minutes sessions	20 – 32 weeks gestation	4 sessions	<ul style="list-style-type: none"> Random assignment n = 37 High compliance in groups 	(60)
Psychotherapeutic	Cognitive-Behavioural session	60 minute session	2 nd – 5 th day postpartum	1 session	<ul style="list-style-type: none"> Randomized, controlled trial n = 258 	(61)
Antidepressant	Sertraline	75 mg/d (start dose 25 mg/d)	Within 24 hours after delivery	17 weeks, then taper for 3 weeks	<ul style="list-style-type: none"> Pilot study (placebo controlled) n = 22 Authors suggested a minimum of 26 weeks administration 	(65)
Dietary Supplement	Calcium	Calcium carbonate tablets 1000 mg bid	Prior to 22 weeks gestation	Until delivery	<ul style="list-style-type: none"> Post hoc analysis n = 4,589 	(66)
Hormonal	Estradiol	Premarin 5 mg bid for 3 d, then tapering (for dosage schedule see Table 2 in [74])	Within 24 hours after delivery	28 days	<ul style="list-style-type: none"> Pilot study n = 4 	(74)
Sleep	Reset Sleep-Wake Cycle		Day 1 postpartum	5 nights	<ul style="list-style-type: none"> Chart review n = 64 	(39)

Taken together, this hints at a biological vulnerability involving the sleep and mood regulation systems.

A new line of research is examining whether re-synchronizing the sleep-wake cycle, i.e., minimizing sleep deprivation in the first week postpartum in women identified as at high risk for PPD will prevent occurrence or re-occurrence. The prophylactic protocol essentially implements a set of guidelines for enhancing sleep after delivery with an extended maternity ward stay, a private room and night rooming-out of the infant. Results of a chart review (n = 64) showed that 21% of 42 women who used the intervention developed PPD, compared with 39% of 22 women who received standard hospital care. In women with a prior history of PPD, similar rates were observed.³⁹ A larger, prospective, randomized controlled trial evaluating this protocol is underway.

Summary & recommendations

Can PPD be easily prevented? The brief answer is, not yet. Taken together, the research points to a strong biologic component underlying its etiology. PPD can occur even in women with no known personal or family psychiatric history, or any of the risk factors. The literature shows that the onset of depression can occur, not merely within a few weeks after delivery, but up to 7 months following parturition.⁸⁷ Thus, close monitoring of mood in the first postpartum year, especially in women with a history of PPD, is crucial.

A few simple questions during routine primary care visits could be effective in identifying women at risk for PPD. These questions should address personal and family psychiatric history, in particular mood disorders and alcoholism, and most importantly, establish the women's current state of mind and mood.²⁵

Abrupt discontinuation of psychotropic regimens during pregnancy should be avoided if possible, to obviate a worsening of psychological health. One observational report found that depressive symptoms significantly worsened in a group of pregnant women that had been taking antidepressants in as little as several weeks following abrupt discontinuation.⁸⁸

Some interventions have shown promise for the reduction of the occurrence of PPD in women at risk (Table 1), but no single strategy has prevented this syndrome in all women identified as such. These studies warrant replication, but at this time all preliminary results should be interpreted with caution until additional controlled studies are available.

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